This document was submitted to EPA by a registrant in connection with EPA's evaluation of this chemical, and it is presented here exactly as submitted.

AMVAC

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March 17, 2000

Via Hand Delivery and Facsimile

Mr. Robert C. McNally, Chief (MC-7508W)
Special Review Branch
Special Review and Reregistration Division
United States Environmental
Protection Agency
1921 Jefferson Davis Highway
Crystal Mall 2
6th Floor
Arlington, VA 22202

Re: DDVP PRA

Dear Mr. McNally:

At our February 10, 2000, meeting, EPA staff stated that a 3-fold FQPA factor would be applied to DDVP based on the trichlorfon data in the pig and guinea pig. At the meeting, we stated our belief that there is a large body of literature on DDVP in the pig. We have since gathered the literature. A list of these studies is appended for EPA's review. Copies of the studies will be provided shortly under separate cover. The literature shows:

- DDVP and trichlorfon have fundamentally different developmental effects in pigs and guinea pigs.
- The DDVP data show no adverse developmental effects in the pig or guinea pig.
  - There are many developmental studies of DDVP in the pig.
  - Several studies show beneficial effects on piglets (pig offspring) of DDVP-treated pregnant sows. These include

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increased body weight of offspring, increased live births, and decreased still births.

- In a study by Stanton *et al.* (1979), pregnant sows were treated with DDVP. Doses that caused cholinesterase activities in blood and plasma to be 30 percent or less of pretreatment levels in the pregnant sows did not result in any change in cholinesterase in the fetuses. This study shows that DDVP does not cross the placental barrier.

- DDVP was without any effect in the Wrathall *et al.* (1980) study of DDVP in the pig. That study was specifically designed to look for the types of brain lesions that trichlorfon produces in the brain and cerebellum of the pig and guinea pig.

- There is no evidence that DDVP or any DDVP metabolites are present in the offspring of treated sows (Potter *et al.*, 1973).

- DDVP is used extensively as a veterinary pharmaceutical in swine (ATGARD®). Despite use of this product over many decades, the literature does not contain reports of adverse developmental effects.

■ The trichlorfon literature shows a consistent congenital defect consisting of cerebellar hypoplasia in offspring of exposed pregnant sows.

- These effects have been experimentally produced and observed in the field.

- There also are several reports of a syndrome consisting of muscular tremor and ataxia in offspring of exposed sows. These effects also have been experimentally produced and observed in the field.

- The literature shows a marked increase in mortality in the offspring of exposed sows.
- The specific sensitive period for exposure of pregnant sows has been identified (Pope *et al.*, 1986).
- There are trichlorfon and trichlorfon metabolites in the fetuses of treated sows (Berge *et al.*, 1986).

- The trichlorfon developmental effects have not been observed in DDVP studies. Moreover, the data show that DDVP increases live births and decreases still births.
- The data show that trichlorfon developmental effects are similar in the pig and guinea pig (Berge *et al.*,1987a, b; Knox *et al.*,1978).
- The Mehl *et al.* (1994) study cannot be used to assess DDVP developmental effects, because the only litter that showed effects was the offspring of a mother who had been injected with maternally lethal levels.

We believe the appended studies require EPA to reassess its proposed application of the 3-fold FQPA safety factor. Amvac believes the appended studies, together with the negative rat and rabbit developmental studies already accepted by EPA, support a conclusion that DDVP has no adverse developmental toxicity effects and thus that no FQPA safety factor is warranted. We look forward to discussing this with you at your earliest convenience.

Sincerely,

Ian S. Chart/ajm

Ian S. Chart
Director of Regulatory Affairs

Attachment
cc: Mr. Jack E. Housenger (w/attachment)(via hand delivery and facsimile)

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Anderson, R.H. and R.G. Wahlstrom. (1970). Effects of energy intake and dichlorvos during gestation on reproductive performance of gilts and some chemical characteristics of the offspring. *J Anim Sci* 13:907-916.

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Potter, J.C., A.C. Boyer, R.L. Marxmiller, R. Young and J.E. Loeffler. (1973). Radioisotope residues and residues of dichlorvos and its metabolites in pregnant sows and their progeny dosed with dichlorvos- 14 C or dichlorvos- 36 C1 formulated as PVC pellets. *J Agric Food Chem* 21(4):734-8.

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